SUMMARY OF CLAIMS

Claims 1-5, 7-9, 13, 14 and 58 are rejected. Claims 6, 10-12, 15-61 are cancelled. Claims 1-5, 7-9, 13 and 14 are amended. Claims 62-78 are new. Claims 1-5, 7-9, 13, 14 and 62-78 are pending. Reconsideration is respectfully requested in light of the following remarks.

REMARKS

I. Examiner Interview

Applicants wish to thank Examiner Larry Riggs and Supervisory Patent Examiner Majorie Moran for extending the courtesy of an Examiner Interview on August 5, 2009 to Applicants' representative Paul Borchardt. Applicants appreciate the opportunity the Interview provided to discuss the §101 rejection and possible claim amendments to overcome the rejection. Furthermore, Applicants appreciate the chance to distinguish the instant invention over the Hughes reference.

II. No New Matter

No new matter is introduced by way of the amended claims as support for the claims can be found throughout the specification. More specifically, support for can be found for individual limitations or claims as follows:

Support for a computer system as recited in claim 1 is found at least in paragraph 66 and in claims 59 and 61 as originally filed.

Support for a second database for a knowledge base of scientific findings as recited in claim 62 is found at least in paragraph 45.

Support for the knowledge base being a frame-based knowledge base as recited in claim 63 is found at least in paragraph 45.

Support for the system being further configured to compare disease-related pathways with data obtained from gene expression studies or a manually entered gene list as recited in claim 64 is found on at least in claims 15 and 17 as originally filed.

Support for gene expression studies comprising differential gene expression studies or microarray studies as recited in claim 65 is found at least in paragraph and claims 15, 17 and 26 as originally filed.

Support for claim 66 is found at least in claim 15 as originally filed.

Support for claim 67 is found at least in claim 16 as originally filed.

Support for claim 68 is found at least in claim 18 as originally filed.

Support for claim 69 is found at least in claim 1 as originally filed.

Support for claim 70 is found at least in claim 21 as originally filed.

Support for claim 71 is found at least in claim 22 as originally filed.

Support for claim 72 is found at least in claim 23 as originally filed.

Support for claim 73 is found at least in claim 26 as originally filed.

Support for claim 74 is found at least in claim 27 as originally filed.

Support for claim 75 is found at least in claim 28 as originally filed.

Support for claim 76 is found at least in claim 29 as originally filed.

Support for claim 77 is found at least in claim 30 as originally filed.

Support for a networked computer system as recited in claim 79 is found in at least paragraph 66.

III. Claim Rejections 35 USC §112

Claims 1-5, 7-9, 13 and 14 are rejected under 35 USC §112, second paragraph, for alleged indefiniteness. The rejection is now moot as Applicants have amended claim 1 to recite "querying the database to identify disease-related pathways." The word "pathway" was inadvertently dropped from the claim in Applicants' response to the Office Action of September 18, 2008, so Applicants have now amended the claim to add back the dropped word.

IV. Claim Rejections under 35 U.S.C. §101

Claims 1-5, 7-9, 13, 14, and 58 are rejected under 35 U.S.C. §101 for allegedly being directed to non-statutory subject matter. More specifically, it is alleged that the instant claims are drawn to a method of identifying a drug discovery target that is not tied to a particular machine or

apparatus or does not transform a particular article into a different state or thing. Applicants traverse the rejection.

The rejection is now moot as Applicants amended claims 1-5, 7-9, 13 and 14 to recite a computer system for identifying a drug discovery target. Consequently, the amended claims recite a tangible apparatus and not an allegedly intangible process. Therefore, Applicants respectfully request the withdrawal of the rejection of claims 1-5, 7, 8, 13, 14, and 58 under 35 U.S.C. 101.

V. Claim Rejections under 35 U.S.C. §102

Claims 1-5, 7, 8, 13, 14, and 58 are rejected under 35 U.S.C. 102(a) for allegedly being anticipated by Hughes et al. (Cell, 2000, 102, 109-126). Applicants traverse the rejection.

Applicants respectfully contend that Hughes et al. do not teach, disclose or suggest at least the storing of genomics information in a database as an ontology. Applicants defined an ontology as a specific database organization. The specification discloses in paragraph 0045 that "[a]n ontology is a multiple-hierarchical representation of the taxonomy and formal concepts and relationships relevant to the domain of interest." As further disclosed in paragraphs 0046 to 0047:

> In this illustrative ontology, the primary organizational grouping is called a class. A class represents a group of things that share similar properties. For example, in the ontology described herein, one class is human cells, which class includes lung cells, skin cells, brains cell and so on. Each of the members of a class is an "instance" of that class, which instances represent single items or elements belonging within the specified class. Thus, an individual blood cell is an instance of the class of human cells.
> The relationships between different instances in the ontology are defined by "slots." Slots can be thought of as the verbs that relate two classes. For example, pancreatic Beta cells have a slot, "produce," linking them to insulin. A "facet" represents more detailed information about a "slot" and can in some cases restrict the values that a slot can have when related to specific instances of a class. The slots and facets define and structure the taxonomic relationships and partonomic relationships between classes.

As illustrated in Figure 1, an ontology is a hierarchically representation of a class that is further comprised of one or more subclasses, each of which may be further comprised of additional subclasses, and so forth. The second order subclasses in Figure 1 represent biological compositions classified by composition type, "Biological Thing by Composition"; biological compositions

classified by function, "Biological Thing by Function"; changes in processes, "Direction of Change Process"; and particular biological phenomena, "Biological Temporal Thing."

Within the second order subclass of Biological Thing by Composition is the fourth order subclass "Protein" that has as an instance "Bax Human Protein." Similarly, within the second order subclass of Biological Thing by Function is the sixth order subclass "Ganglion Cell" that has as an instance, "Dorsal Root Ganglion Cell." Likewise, within the second order subclass of Direction of Change Process is the third order class "Affect Process" with the instance, "Increase Process." Additionally, within the second order subclass of Biological Temporal Thing is the fourth order subclass "Cell Death" with "Apoptosis" as an instance.

The relationship "slots" between the instances above are illustrated Figure 1 as the dotted lines that connect the bolded boxes. Here, the protein instance, "Bax Human Protein" is connected to the Ganglion Cell instance "Dorsal Root Ganglion Cell" that in turn is connected to the Affect Process instance, "Increase Process" that is further connected to the Cell Death" instance, "Apoptosis." These relations represent part of the relationships between individual concepts extracted from a scientific finding (fact) as disclosed in paragraph 0049, that were placed into the appropriate subclasses of the ontology.

Rather than disclosing a database organizational structure, Applicants respectfully contend that the agglomerative hierarchical clustering of Hughes et al. is a statistical method used to classify items based on similarities. In Hughes et al., it is experiments and gene responses that are classified. (page 124, right column, "Clustering and Error Model") As Exhibits #1 and #2 demonstrate, agglomerative hierarchical clustering is not an ontology and does not feature at least the slots of an ontology thereby preventing the representation of relationships between particular subclass instances.

Since the genomics information is stored as an ontology, a feature not disclosed or suggested in Hughes et al., Applicants submit that the instant invention is novel over Hughes et al. Consequently, Applicants respectfully request the withdrawal the rejection of claims 1-5, 7, 8, 13, 14, and 58 under 35 U.S.C. §102(a).

CONCLUSION

Applicants submit that this paper fully addresses the Office Action mailed September 18, 2008. Should the Examiner have any question, the Examiner is encouraged to telephone the undersigned agent or attorney Paul Borchardt (Reg. No. 53,999) at (650) 565-3895.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit account No. 23-2415 (Attorney Docket No.: 27763-705.501) for any matter in connection with this response, including any fee for extension of time, which may be required.

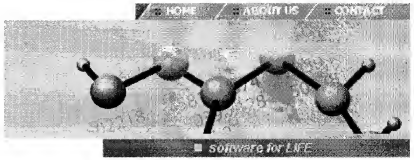
Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

Dated: September 14, 2009

By: _____
Paul Borchardt, Reg. No. 53,999

650 Page Mill Road
Palo Alto, CA 94304-1050
(650) 493-9300
Client No. 021971



Agglomerative Hierarchical Clustering Overview

Overview

Agglomerative hierarchical clustering is a bottom-up clustering method where clusters have sub-clusters, which in turn have sub-clusters, etc. The classic example of this is species taxonomy. Gene expression data might also exhibit this hierarchical quality (e.g. neurotransmitter gene families). Agglomerative hierarchical clustering starts with every single object (gene or sample) in a single cluster. Then, in each successive iteration, it agglomerates (merges) the closest pair of clusters by satisfying some similarity criteria, until all of the data is in one cluster.

The hierarchy within the final cluster has the following properties:

- Clusters generated in early stages are nested in those generated in later stages.
- Clusters with different sizes in the tree can be valuable for discovery.

A Matrix Tree Plot visually demonstrates the hierarchy within the final cluster, where each merger is represented by a binary tree.

Process

- Assign each object to a separate cluster.
- Evaluate all pair-wise distances between clusters (distance metrics are described in Distance Metrics Overview).
- Construct a distance matrix using the distance values.
- Look for the pair of clusters with the shortest distance.
- Remove the pair from the matrix and merge them.
- Evaluate all distances from this new cluster to all other clusters, and update the matrix.
- Repeat until the distance matrix is reduced to a single element.

Advantages

- It can produce an ordering of the objects, which may be informative for data display.

U.S. Appl. No. 10/632,099 Exhibit # 1

- Smaller clusters are generated, which may be helpful for discovery.

Disadvantages

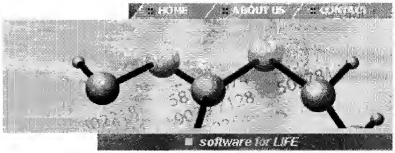
- No provision can be made for a relocation of objects that may have been 'incorrectly' grouped at an early stage. The result should be examined closely to ensure it makes sense.
- Use of different distance metrics for measuring distances between clusters may generate different results. Performing multiple experiments and comparing the results is recommended to support the veracity of the original results.

Divisive Hierarchical Clustering

- A top-down clustering method and is less commonly used. It works in a similar way to agglomerative clustering but in the opposite direction. This method starts with a single cluster containing all objects, and then successively splits resulting clusters until only clusters of individual objects remain. ***GeneLinker™ does not support divisive hierarchical clustering.***

Related Topics:

Clustering Overview
Performing Agglomerative Hierarchical Clustering



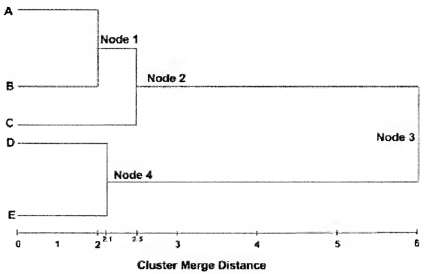
Creating a Matrix Tree Plot

Overview

Tree plots visually highlight clustering relationships. They are indispensable for hierarchical clusterings, and can also be used to view partitional clusterings (K-Means and Jarvis-Patrick), and SOMs.

The matrix tree plot is a combined display of a tree plot and a color matrix. At the top, the plot legend consists of a color gradient above an expression value scale. The default range for the scale is from the minimum to the maximum value contained within the dataset. The cluster tree appears to the right of the color array when samples are clustered, or below it when genes are clustered.

The tree for a hierarchical clustering is a close reflection of the agglomerative algorithm that produced it. Consider gene clustering: two very similar genes are joined at a 'node', representing a cluster. That line is joined to the next nearest gene or sub-cluster by another line a little lower, and so on. In the end, closely related genes tend to appear beside each other in the diagram. (**Note** that the converse is not true - genes appearing beside each other in the tree diagram are only closely related if they are also linked by lines).



In the picture above:

- Cluster Node 1 contains A and B
- Cluster Node 2 contains A, B, and C
- Cluster Node 3 contains A, B, C, D and E

U.S. Appl. No.: 10/632,099 Exhibit #2

- Cluster Node 4 contains D and E
- Cluster Node 1 merged together the 'closest', Cluster Node 4 the next 'closest', and Cluster Node 2 the next 'closest' after that. Cluster Node 3 contains all the items from the entire dataset, representing the cluster with the largest distance between its members.

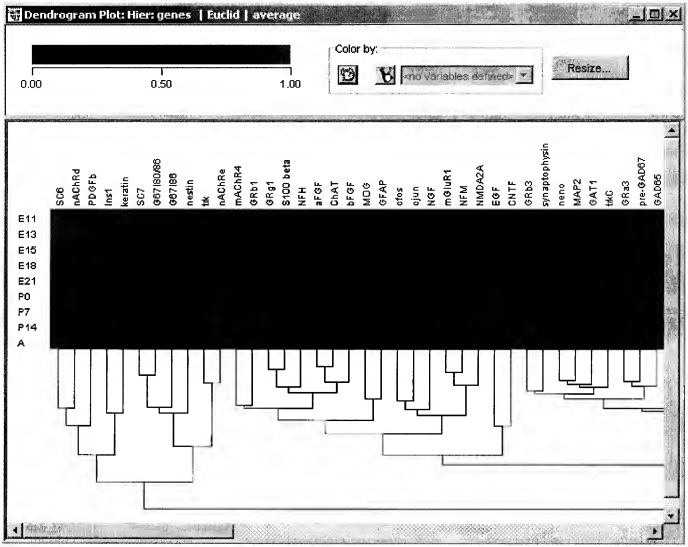
For partitional clustering, there is a separate comb for each cluster, and the combs have only one level (hence the alternative name 'flat clustering'.) All items (genes or samples) in a cluster appear together but no further ordering is done on the items within a cluster.

Actions

1. Double-click a hierarchical or partitional clustering experiment in the **Experiments** navigator. The item is highlighted and a matrix tree plot of the selected item is displayed.

OR

1. Click a hierarchical or partitional clustering, or a SOM experiment item in the **Experiments** navigator. The item is highlighted.
2. Click the **Matrix Tree Plot** toolbar icon  , or select **Matrix Tree Plot** from the **Clustering** menu, or right-click and select **Matrix Tree Plot** from the shortcut menu. A matrix tree plot of the selected item is displayed.



Plot Indicators

As you move the mouse pointer over a gene or sample name, a gray bounding box is drawn around its column or row so you can easily see which tiles belong to it.

The name of selected genes or samples are highlighted in dark blue with white text. It is not possible to select genes and samples concurrently.

Interacting With the Plot

Selecting Items

Displaying a Gene Expression Value

Plot Functions

Profile Matching

Color by Gene Lists or Variables

Exporting an Image

Customizing the Plot

Changing the Gradient Color and Scale

Resizing Cells in a Color Grid

Toggling the Color Grid On or Off

Related Topic:

Creating a Summary Statistics Chart